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09/642,068	08/18/2000	John R. Stuelpnagel	A-68364-1/RMS/DCF	6751

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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 11/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/642,068	STUELPNAGEL ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2004 and 14 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-10,27-31 and 33-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-10,27-31 and 33-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *15062004* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to amendments filed April 22, 2004 and September 14, 2004. Claims 2-10 and 27-31 were previously pending. Applicants amended claims 27, 28, 29 and 30, and added new claims 33-37. Claims 2-10, 27-31 and 33-37 are pending and will be examined.

2. Applicants' amendments and arguments overcame the rejection of claims 27, 30, 31, 3-6 and 9 under 35 U.S.C. 102(e) as anticipated by Beattie. All other rejections are maintained for reasons given in the "Response to Arguments" section below.

Response to Arguments

3. Applicant's arguments filed April 22, 2004 have been fully considered but they are not persuasive.

A) Regarding the rejection of claims 2-10 and 27-31 over Holmes and Beattie, Applicants argue the following:

a) There is no teaching or suggestion in Holmes of generating a pool of oligonucleotides by cleaving the oligonucleotides from the support, because, as stated by Applicants,

> "In this regard, the mere assertion at column 6, lines 36-37 that compounds synthesized on beads provided on a surface may be released upon completion of a synthesis does not teach or suggest generating a pool of different oligonucleotides because the compounds would have likely been released individually."

Applicants further argue that the teachings of Beattie do not cure the deficiency of Holmes, since Beattie does not teach generating pools of oligonucleotides comprising first and second different oligonucleotides.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations

of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

First, the passage of Holmes cited by Applicants very strongly suggests creating pools of different oligonucleotides, since they do not specifically teach individually releasing single types of oligonucleotides, and the Applicants' hypothesis that they would have likely been released individually is just that, since it is not based on the teachings of the reference. In this rejection Beattie is relied upon for the limitation of contacting cleaved oligonucleotides with target nucleic acids, which Holmes teaches implicitly by teaching sequencing by hybridization and using oligonucleotides in bioassyas. Therefore, the combination of Holmes and Beattie teaches and suggests all of the claim elements.

b) Applicants also argue that even if the two references taught all of the claim elements, there is no motivation to combine the references, since Beattie teaches away from the creation of pools of different oligonucleotides. This point was already addressed above, since the fact that Beattie teaches away from having different pools of oligonucleotides has no bearing on the combination of the two references, since Beattie is relied upon for the limitation of contacting cleaved oligonucleotides with target nucleic acids, which Holmes teaches implicitly by teaching sequencing by hybridization and using oligonucleotides in bioassyas.

In conclusion, the rejections are maintained.

Claim interpretation

4. The following interpretation of claim limitations is used to evaluate correspondence between the current claims and prior art:

A) The term " first and second linkers" is interpreted as linkers which may be the same, as there is no requirement that they have to be different.

B) The term "chip" in claim 29 is interpreted as any substrate (it is used interchangeably with "substrate" in the claim. Applicants' definition on page 16, fourth paragraph: "... By "chip" or biochip" herein is meant a planar substrate to which nucleic acids are directly or indirectly attached."

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 2-10, 27-31 and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes (U.S. Patent No. 5,679,773; cited in the office action of August 13, 2002) and Beattie (U.S. Patent No. 6,156,502).

A) Since claims 28 and 29 are species of claims 27 and 30, the newly added claims 33 and 35 are restated versions of claim 27 and the newly added claim 34 is a restated version of claim 28, only steps of claims 28 and 29 are discussed explicitly.

Regarding claims 27-30 and 33-35, Holmes teaches a method of synthesis and release of nucleic acids, the method comprising:

a) providing a substrate and a population of oligonucleotides, said population comprising at least first and second different oligonucleotides, respectively, said first and second oligonucleotides being immobilized to first and second beads, respectively, through first and second cleavable linkers, respectively, said first and second beads being distributed on said substrate (Holmes teaches providing a substrate and compounds, such as oligonucleotides, synthesized on solid supports (= substrate), which may contain wells. Compounds are synthesized on beads distributed on the

surface of the support (Abstract; col. 5, lines 64-67; col. 6, lines 26-37; col. 19, lines 58-67; col. 20, lines 1-7; col. 22, lines 11-16). Holmes teaches preparation of high-density arrays of diverse oligonucleotides (col. 2, lines 1-7; col. 10, lines 15-25), therefore Holmes teaches at least first and second oligonucleotides.);

b) cleaving said first and second linkers, thereby releasing said first and second subpopulations from said first and second beads, thereby generating a pool of oligonucleotides comprising said first and second oligonucleotides (Holmes teaches cleaving the oligonucleotide probes from the support (col. 6, lines 36, 37; col. 12, lines 6-16). Since Holmes teaches multiple diverse oligonucleotides, cleavage generates a pool of oligonucleotides comprising first and second different oligonucleotides, anticipating this limitation.) ; and

c) contacting said first and second oligonucleotides with a composition comprising at least a first and second target nucleic acid, whereby said first and second target nucleic acids hybridize with said first and second oligonucleotides whereby said target nucleic acids are detected (Holmes teaches contacting the oligonucleotide array with a sample or using released oligomers in bioassays (col. 10, lines 18-21; col. 12, lines 15, 16). Holmes teaches using arrays for sequencing by hybridization (col. 1, lines 61-67).)

Regarding claim 2, Holmes teaches nucleic acids which are synthesized with DNA or RNA binding sequences which act as "receptors" for other nucleic acid sequences (col. 5, lines 64-66). Holmes does not specifically teach oligonucleotides with known sequences, but since they are synthesized to bind a specific sequence, their sequences must be known. Thus Holmes anticipates limitation of claim 2.

Regarding claim 3, Holmes teaches attaching labels to compounds synthesized on a substrate (col. 20, lines 33-67) and labeled beads attached to oligonucleotides (col. 10, lines 6-14).

Regarding claim 4, Holmes teaches labeled beads attached to oligonucleotides, where the beads are unique to each oligonucleotide or probe (col. 10, lines 6-14), anticipating the limitation of first and second oligonucleotides having different labels.

Regarding claims 5 and 31, Holmes teaches oligomers (e.g. oligonucleotides) attached to the solid support by covalent linkers, which are photochemically or chemically cleavable (col. 11, lines 23-67; col. 12, lines 6-16; col. 20, lines 7-32).

Regarding claims 6 and 9, Holmes teaches synthesis of oligonucleotides on a substrate (col. 6, lines 26-37; col. 22, lines 11-16).

Regarding claim 7, Holmes teaches substrate comprising discrete sites, such as wells, trenches, etc. (col. 6, lines 27-32).

Regarding claim 8, Holmes teaches beads distributed on a substrate and synthesis of oligomers on the beads (col. 6, lines 34-37; col. 9, lines 30-67; col. 10, lines 1-5).

Regarding claim 10, Holmes teaches synthesis of compounds by photolitography (col. 7, lines 23-40; col. 18, lines 1-67).

Regarding claim 36, Holmes teaches glass or silicon oxide as solid supports (col. 15, lines 43, 44) and a variety of other materials (col. 19, lines 58-67; col. 20, lines 1-7).

Regarding claim 37, Holmes teaches a flat rigid or semi-rigid substrate (col. 6, lines 26-28) and attachment of oligonucleotides to the surface (col. 19, lines 35-48; col. 5, lines 64-67), therefore, according to Applicants' definition, Holmes teaches a chip.

B) Holmes teaches oligonucleotide arrays, sequencing by hybridization and using cleaved oligonucleotides in bioassays, but does not specifically teach contacting the oligonucleotides with target nucleic acids.

C) Beattie teaches a method of oligonucleotide fingerprinting (ASOF), in which oligonucleotides cleaved from a solid support are contacted with a sample comprising target nucleic acids (Fig. 6; col. 8, lines 30-39; col. 12, lines 57-64). The target nucleic acids are contained in genomic DNA (col. 3, lines 14-27) or total RNA (col. 4, lines 14-16).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the assay of Beattie to use oligonucleotides cleaved from solid support of Holmes. The motivation to do so, provided by Beattie, would have been that the ASOF assay was used in polymorphic marker analysis, species identification and transcriptional profiling without the need for electrophoresis (Abstract).

7. No claims are allowed.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

TS
November 16, 2004

JEFFREY FREDMAN
PRIMARY EXAMINER
11/18/04